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High Production Volume (HPV) Challenge Program

DIMETHYL DISULFIDE

(CAS# 624-92-0)

Test Plan

Arkema Inc.
2000 Market Street
19103 Philadelphia, PA

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EXECUTIVE SUMMARY

Arkema Inc has volunteered to sponsor dimethyl disulfide (DMDS, CAS# 624-92-0) in the USEPA HPV program. The DMDS Test Plan is being submitted to fulfill the United States Environmental Protection Agency (USEPA) High Production Volume (HPV) Challenge Program commitment for DMDS.

Data from company proprietary files, peer-reviewed literature, and/or calculated endpoints using widely accepted computer modeling programs have been identified for purposes of this program. Robust summaries of the available data are included in the attached IUCLID. The following table summarizes the available data and proposed testing for DMDS.

Table 1: Matrix of Available and Adequate Data on DMDS

"SIDS ENDPOINT"	Data Available Y/N	Testing Planned? Y/N
Physical and Chemical Data		
Melting Point	Y	N
Boiling Point	Y	N
Vapor Pressure	Y	N
Partition Coefficient	Y	N
Water Solubility	Y	N
Environmental Fate		
Photodegradation	Y	N
Stability in Water (Hydrolysis)	N	Y
Transport/Distribution	Y	N
Biodegradation	Y	N
Ecotoxicity		
Acute/Prolonged Toxicity to Fish	N	Y
Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	Y	N
Acute Toxicity to Aquatic Plants (Algae)	Y	N
Toxicity		
Acute Toxicity (Oral)	Y	N
Acute Toxicity (Dermal)	Y	N
Acute Toxicity (Inhalation)	Y	N
Repeated Dose	Y	N
GeneticToxicity *in vitro* – Gene Mutation	Y	N
Genetic Toxicity *in vitro* – Chromosomal Aberration	Y	N
Reproductive Toxicity Developmental Toxicity	Y	N

Note: **The data used to characterize the OECD SIDS endpoints for substances in this Test Plan were identified either in company proprietary files, peer-reviewed literature, and/or calculated using widely accepted computer modelling programs. All data were evaluated for study reliability in accordance with criteria outlined by the USEPA (1999a). Only studies that met the reliability criteria of "1" (reliable without restrictions) or "2" (reliable with restrictions) were used. Additional data are also included in the IUCLID (International Uniform Chemical Information Dataset) attached in Annex I. A more detailed discussion of the data quality and reliability assessment process used to develop this test plan is provided in Annex II.**

1.1   Physico-Chemical properties

DMDS is a pale yellow liquid with a strong garlic like odor.   Experimental data for the physical chemical parameters are available and reported in EPIWIN[©] (USEPA, 2004) and are provided in the following table.

Table 2.   Physicochemical Data

Parameter	*Value*
Melting Point	-85ºC [1]
Boiling Point	110ºC [1]
Vapor Pressure	29.3 hPa
Kow Partition Coefficient	1.77[1]
Water Solubility (mg/l)	2500[1]

[1]EPIWIN v3.12 – Syspro database

Conclusion

  Adequate data are available for the HPV physical/chemical property endpoints. No additional testing for the HPV program is proposed.

GENERAL INFORMATION ON EXPOSURE

1.2   Production Volumes and Use Pattern

DMDS is on EPA's high production volume list indicating it is manufactured and/or imported at greater than 1 million pounds per year according to the toxic inventory update rule (IUR).

1.2.1   Use Pattern:

DMDS has several industrial uses. It is used in the oil industry as a sulfiding/presulfiding agent to activate catalysts of hydrotreating units, to reduce the number of decoking operations in the petrochemical industry, as a chemical intermediate in the fine chemical industry, and as an anti-corrosive in metallurgy.

1.3   Environmental Exposure and Fate

1.3.1   Photodegradation

The photodegradation of DMDS was evaluated using EPIWIN 3.12. The half life of DMDS was calculated to be 0.565 hours based on the experimental rate constant of 227 x E-12 cm3/molecule-sec.

Conclusion

Adequate data are available to assess the photodegradation of DMDS. No additional studies are proposed for the HPV program.

1.3.2 Stability in Water

EPIWIN was unable to calculate a hydrolysis rate for DMDS. A hydrolysis study is proposed for DMDS.

1.3.3 Transport between Environmental Compartments

The transport of DMDS between environmental compartments was assessed by fugacity modeling using EPIWIN (v3.12). Results are listed in the table below:

Table 3. Fugacity Results for DMDS

Compartment	Mass amount (%)	Estimated half life (hr)
Air	1.01	1.13
Water	58.1	360
Soil	40.8	360
Sediment	0.168	3.24x e003

1.3.4 Biodegradation

DMDS was not readily biodegradable when evaluated according to OECD 301D. The degradation was less than 10% following 28 days exposure.

Conclusion

Adequate data are available to assess the biodegradation of DMDS. No additional studies are proposed for the HPV program.

2 HUMAN HEALTH HAZARDS

2.1.1 Acute Toxicity

Single exposure (acute) studies indicate DMDS is moderately toxic if swallowed (rat; 290 mg/kg < LD50 < 500 mg/kg), no more then slightly toxic if absorbed through skin (rabbit LD50 >2,000 mg/kg), and slightly toxic if inhaled (rat 4-hr LC50 805 ppm).

Conclusion

Adequate data are available to assess the acute toxicity of DMDS and no additional studies are proposed.

2.1.2 Repeated Dose Toxicity

DMDS was evaluated in a 90-day repeated dose study on rats according to OECD guidelines. This study featured inhalation dosing, measurement of mortality, body weight changes, food consumption, hematological and blood biochemical examinations, urinalysis, organ weights, histopathology and a functional observational battery. Rats were exposed whole body to 0, 10, 50, 150, and 250 ppm DMDS for 6 hours per day for 90 days. Satellite groups were evaluated

following a 2-week recovery period. Results from this study showed decreased body weights, food consumption, hypoactivity, changes in white blood cell counts, reduced thymus gland weight and increased liver weight. Reversible microscopic changes were noted in the nasal mucosa.

Conclusion

Adequate data are available to assess the reproductive toxicity of DMDS. No additional testing is proposed for purposes of the HPV program.

2.1.3   Mutagenicity

Several reliable genetic toxicity studies are available for DMDS. Predominantly negative results were obtained with DMDS when tested *in vitro* (negative bacterial and mammalian mutagenicity assays, negative DNA damage and repair, ambiguous positive in vitro chromosome aberration study using human lymphocytes). Negative results were obtained when DMDS was evaluated *in vivo* (mouse micronucleus, unscheduled DNA synthesis).

Conclusion

Adequate data are available to assess the genetic toxicity of DMDS. No additional testing is proposed for purposes of the HPV program.

2.1.4   Toxicity for Reproductive/Developmental Toxicity

Reproductive Toxicity

The 90 day repeated dose toxicity study will be used to assess the reproductive toxicity of DMDS. Reproductive organs examined in this study included the epididymus, prostate, and testes in males and ovaries and uterus in females. No lesions were reported.

Developmental Toxicity

A Developmental Toxicity test was completed for DMDS in Sprague-Dawley rats following OECD Guideline 414 "Teratogenicity." DMDS was administered by inhalation to 0, 5, 15, and 50 ppm on gestation days 6 to 15. Maternal toxicity was noted at 15 and 50 ppm. No evidence of developmental toxicity was observed. No additional studies are proposed.

Conclusion

Adequate data are available to assess the reproductive and developmental toxicity of DMDS. No additional testing is proposed for the HPB program.

3   HAZARDS TO AQUATIC ORGANISMS

DMDS has been evaluated in an acute daphnia immobilization and algal growth inhibition studies. DMDS is moderately toxic to daphnia with a 48 hour EC50 value of 7 mg/l. DMDS is slightly toxic to *Selenastrum capricornutum* alga with a 72 hour EC50 of 35 mg/l. No data are available for acute fish and alga. No data are available to assess the acute fish toxicity and an acute fish toxicity (OECD guideline 203) is proposed for DMDS.

Conclusion

Adequate data are available to assess the aquatic toxicity of DMDS to daphnia and alga but not fish. An acute fish toxicity study is proposed (OECD guideline 203) for DMDS.

References

Atofina, 2005. IUCLID Data Set, CAS No. 624-92-0 dimethyldisulfide. Atofina, Paris, France.

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Organisation for Economic Co-operation and Development (OECD) Secretariat. 2002. *Manual for Investigation of HPV Chemicals* (November 2002).

U.S. Environmental Protection Agency (USEPA), Office of Pollution Prevention and Toxics. 1998. Guidance for Meeting the SIDS Requirements: Chemical Right-to-Know Initiative.

USEPA, Office of Pollution Prevention and Toxics. 1999b. Draft Determining the Adequacy of Existing Data.

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ANNEX I: DIMETHYL DISULFIDE IUCLID

See attached IUCLID documents.

ANNEX II: DATA QUALITY ASSESSMENT

Available environmental, ecotoxicity, and mammalian toxicity studies were reviewed and assessed for reliability according to standards specified by Klimisch et al., (1997), as recommended by the USEPA (1999a) and the OECD (OECD, 2002). The following reliability classification (Klimisch rating) has been applied to each study assessed:

- *1 = Reliable without Restriction* – Includes studies that comply with USEPA- and/or OECD-accepted testing guidelines and were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented;

- *2 = Reliable with Restriction* – Includes studies that were conducted according to national/international testing guidance and are well documented. May include studies that were conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters that are well documented and scientifically valid but vary slightly from current testing guidance. Also included in this category were physical-chemical property data obtained from reference handbooks, as well as environmental endpoint values obtained from an accepted method of estimation (e.g., USEPA's EPIWIN estimation program);

- *3 = Not Reliable* – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or in which documentation is insufficient; and,

- *4 = Not Assignable* – This designation is used in this dossier for studies that appear scientifically valid but for which insufficient information is available to adequately judge robustness.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this dossier. Those key studies selected for inclusion are considered typical of the endpoint responses observed in other studies of a similar nature and design that were identified during our search of the literature.